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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/463,590	04/20/00	LANDRY S	07005/00302

EXAMINER	
DECLOUX A	
ART UNIT	**PAPER NUMBER**
1644	8

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DATE MAILED: 09/25/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.	Applicant(s)
09/463,590	Landry, Samuel J.
Examiner	**Art Unit**
DeCloux, Amy	1644

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 5, 2001*

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-19 and 58* is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-19 and 58* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

1. Applicant's election without traverse of Group I (claims 1-8, and 11-19) in Paper No. 127, mailed 7-2-2001, is acknowledged. Applicant's election of the following species is also acknowledged: 1) HIV GP120, 2) insertion of human hsp mobile loop, 3) human, 4) sixteen amino acids, 5) cathepsin S 6)average hydrophobicity value that is lower than the average hydrophobicity value of said altered protein, 7) average hydrophobicity value that is higher than the average hydrophobicity value of said altered protein reducing cytotoxic T cell activity.

At applicant's request and upon reconsideration, claims 9-10 will also be examined with group I as well as newly added claim 58.

2. Formal drawings and/or photographs have been submitted which fail to comply with 37 CFR 1.84. Please see the attached PTO-948 form.

3. Applicant should amend the first line of the specification to mention the status of the priority documents.

4. The specification is objected to because incorporation of subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference. See MPEP 608.01(p), paragraph I regarding incorporation by reference. Therefore the embedded hyperlinks and/or other forms of browser-executable code disclosed on pages 16, 17 and 26, and any others not noted, of the instant specification are impermissible and require deletion. Where the hyperlinks and/or other forms of browser-executable codes are part of applicant's invention and are necessary to be included in the patent application in order to comply with the requirements of 35 U.S.C. 112, first paragraph, and applicant does not intend to have these hyperlinks be active links, then this objection will be withdrawn and the Office will disable these hyperlinks when preparing the patent text to be loaded onto the PTO web database.

5. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-13, 15-17 and 18-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

In the instant case, the specification does not convey to the artisan that the applicant had possession, at the time of invention, of the claimed unstable polypeptide sequence (with the exception of the unstable polypeptide segment having the properties recited in claims 14 and 18) comprised by a method for stimulating an immune response specific toward a naturally occurring protein as recited in Claims 1-13, 15-17 and 18-19. The instant claims merely recite said sequence in terms of a property (unstable) but does nothing to describe what is unstable and what is stable. Due to this broad definition of the term unstable polypeptide segment, said term (with the exception of the the unstable polypeptide segment in the terms recited in claims 14 and 18) Fails to meet the written description provision of 35 USC 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See Vas-Cath, page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath, page 1116.).

The skilled artisan cannot envision all the unstable polypeptide sequences (except those recited in claims 14 and 18) that could be inserted by artifice in the recited aletered protein, and therefore conception cannot be not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

Therefore, only the unstable polypeptides having the properties recited in claims 14 and 18 but not the full breadth of the instant claims, meets the written description provision of 35 USC 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

8. Claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for stimulating an immune response specific toward a naturally occurring protein comprising administering an altered protein or polypeptide fragment thereof derived from said naturally occurring protein, wherein an unstable polypeptide segment has been inserted by artifice into said altered protein, wherein immunogenicity of the naturally occurring protein is increased and wherein said segment has the properties recited in instant claims 14 or 18, does not reasonably provide enablement for the broader recitation of a method for stimulating an immune response specific toward a naturally occurring protein comprising administering altered protein or polypeptide fragment thereof derived from said naturally occurring protein, wherein any unstable polypeptide segment has been inserted by artifice into said altered protein, and/or wherein immunogenicity of the naturally occurring protein is not increased. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. .

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed in claims 1-19 without an undue amount of experimentation. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the large number of unstable polypeptide segments, known and unknown, broadly encompassed by the claims.

The instant specification provides insufficient guidance for a method encompassing any unstable polypeptide segment other than that recited in claims 14 or 18. It is known in the art that even single amino acid change or difference in a protein's amino acid sequence can have dramatic effects on the protein's function, as evidenced by the teachings of Abaza et al (J. Of Protein Chemistry, 11(5):433-444, 1992). Abaza et al show that even a single amino acid difference in an antigen may effect antibody binding by teaching that an amino acid substitution of myoglobin outside the epitope recognized by a monoclonal antibody causes the myoglobin to be unreactive with said antibody, (see entire article, especially the Abstract). Further Hubbard et al (IDS) teach in Protein Science (1994) that specific conformations are required for cleavage of limited proteolytic sites to enable the protease to bind and cut (see entire article including the Abstract). Since antigenic epitopes are generated through proteolysis in the cell, a proper conformation must be acheived in the protein for proteolysis, and therefore inserting any instable segment may not lead to a proper conformation for proteolyis by endogenous proteases. Therefore predicting which unstable polypeptide segment other than that recited in claims 14 or 18, that is effective in providing a proteolytic site in a naturally occurring protein which will stimulate an immune response presumably by generating peptide fragments for presentation by MHC molecules, would require undue experimentation.

In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the

specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention and this is not sanctioned by the statute.

9. Claim 58 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 58 recites a method for stimulating an immune response toward a naturally occurring protein comprising administering an altered HIV gp120 protein wherein a human HSP mobile loop has been inserted by artifice into said altered HIV gp120 protein. However it is not clear how increasing the immunogenicity of the gp120 protein by said modification (such as inserting an HSP mobile loop into the sites in gp120 as indicated by Figure 15 of the instant specification) stimulates an immune response toward any naturally occurring protein other than gp120 itself. There is insufficient guidance and direction that said insertions even stimulate an immune response to any protein , including gp120, and further, there is insufficient guidance and direction how the recited modification of gp120 would stimulate an immune response to any other protein. In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Based upon said insufficient guidance in the instant specification, it would require an undue amount of experimentation on the part of one skilled in the art to use the claimed altered gp120 polypeptide in the recited method of stimulating the immune response against a naturally occurring protein.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention and this is not sanctioned by the statute.

10. No claim is allowed. However there does appear to be allowable subject matter, if for example, if claim 1 incorporated the limitations of claim 9 and claims 14-15 because the prior art does not appear to teach or suggest a method for stimulating an immune response specific toward a naturally occurring protein comprising administering an altered protein or polypeptide fragment thereof derived from said naturally occurring protein, wherein an unstable polypeptide segment has been inserted by artifice into said altered protein, wherein immunogenicity of the naturally occurring protein is increased and wherein said segment has the properties recited in instant claims 14 or 18.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy DeCloux whose telephone number is (703) 306-5821. The examiner can normally be reached Monday through Friday from 9:00 am to

6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Amy DeCloux, Ph.D.
Patent Examiner,
September 24, 2001

David A. Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
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